

What is claimed is:

1. A method for detecting a senescent cell, which comprises measuring a relative alteration to young cell in a signal or molecular species involved in signal transduction, wherein the alteration in signal or molecular species is one or more selected from the group consisting of:

- (a) a reduction in Ca^{2+} oscillation;
- (b) a reduction in expression of F-actin;
- (c) a reduction in activity of phospholipase C;
- (d) a reduction in activity of phospholipase D;
- (e) a reduction in expression or phosphorylation of platelet-derived growth factor receptor;
- (f) a reduction in phosphorylation of phospholipase C- γ 1;
- (g) a reduction in expression of phospholipase D 1;
- (h) a reduction in expression of EDG-2;
- (i) a reduction in expression of EDG-7;
- (j) a reduction in expression of Gi1;
- (k) a reduction in expression of Gi2;
- (l) a reduction in expression of Gi3;
- (m) an increase in activity or expression of adenylyl cyclase;
- (n) a reduction in activity or expression of phosphodiesterase;
- (o) an increase in activity of protein kinase C;
- (p) an increase in activity or expression of protein kinase

A;

(q) an increase in phosphorylation of CREB; and

(r) an increase in cAMP content.

5 2. The method according to claim 1, wherein the signals or molecular species of (a)-(g) are involved in signal transduction triggered by platelet-derived growth factor.

10 3. The method according to claim 1, wherein the signals or molecular species of (h)-(r) are involved in signal transduction triggered by lysophosphatidic acid.

4. The method according to claim 1, wherein the senescent cell is derived from human cell.

15 5. The method according to claim 4, wherein the human cell is fibroblast.

20 6. The method according to claim 3, wherein the adenylyl cyclase with increased expression in senescent cell is adenylyl cyclase II, adenylyl cyclase IV or adenylyl cyclase VI.

7. The method according to claim 3, wherein the phosphodiesterase with reduced expression in senescent cell is phosphodiesterase 4B.

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8. The method according to claim 3, wherein the protein kinase A with increased expression in senescent cell is Ca, RI α or RI β subunit thereof.

9. A method for modulating cellular senescence comprising treating a senescent cell with the effective amount of an inhibitor of adenylyl cyclase, an inhibitor of protein kinase A, an inhibitor of protein kinase C or an activator of Gi protein.

10. The method according to claim 9, wherein the inhibitor of adenylyl cyclase is selected from the group consisting of 2',5'-dideoxyadenosine, cis-N-(2-phenylcyclopentyl)azacyclotridec-1-en-2-amine and 9-(tetrahydro-2'-furyl)adenine.

11. The method according to claim 9, wherein the inhibitor of protein kinase A is selected from the group consisting of adenosine 3',5'-cyclic phosphorothiolate, 8-bromo-adenosine 3',5'-cyclic monophosphorothioate, 4-cyano-3-methylisoquinoline, 1-(5-isoquinolinesulfonyl)-2-methylpi

perazine, N-[2-(methylamino)ethyl]-5-isoquinolinesulfonamide, isoquinolinesulfonamide, N-(2-aminoethyl)-5-isoquinolinesulfonamide, N-[2-((p-bromocinnamyl)amino)ethyl]-5-isoquinolinesulfonamide and (5-isoquinolinesulfonyl)piperazine.

12. The method according to claim 9, wherein the inhibitor of

protein kinase C is selected from the group consisting of 2-[1-(3-dimethylaminopropyl)-1H-indol-3-yl]-3-(1H-indol-3-yl)-maleimide, 2-[1-[2-(1-methylpyrrolidino) ethyl]-1H-indol-3-yl]-3-(1H-indol-3-yl)maleimide, 2-[1-(3-aminopropyl)-1H-indol-3-yl]-3-(1H-indol-3-yl)maleimide, 2,3-bis(1H-indol-3-yl)maleimide and 2,3-bis(1H-indol-3-yl)-N-methylmaleimide.

13. The method according to claim 9, wherein the activator of Gi protein is selected from the group consisting of N₆-cyclopentyladenosine, 5-chloro-N₆-adenosine, 2-[p-(2-carboxyethyl) phenethylamino]-5'-N-ethylcarboxamido adenosine, oxymetazoline, prazosin, 2-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-4,4-dimethyl-(2H,4H)-isoquinoline-1,3-dione, cannibinol, MGSA, 3-aminopropylphosphinic acid, galanin, quisqualate, sumatriptan, melatonin, (5,7,8)-(-)-N-methyl-[7-(1-pyrrolidinyl)-1-oxaspiro(4,5)dec-8-yl]benzeneacetamide and pertussis toxin.

14. The method according to claim 9, wherein the senescent cell is derived from human cell.

15. The method according to claim 12, wherein the human cell is fibroblast.

16. A composition for modulating cellular senescence of a

senescent cell comprising the effective amount of an inhibitor of adenylyl cyclase, an inhibitor of protein kinase A, an inhibitor of protein kinase C or an activator of Gi protein.

5 17. The composition according to claim 16, wherein the inhibitor of adenylyl cyclase is selected from the group consisting of 2',5'-dideoxyadenosine, cis-N-(2-phenylcyclopentyl)azacyclotridec-1-en-2-amine and 9-(tetrahydro-2'-furyl)adenine.

10 18. The composition according to claim 16, wherein the inhibitor of protein kinase A is selected from the group consisting of adenosine 3',5'-cyclic phosphorothiolate, 8-bromo-adenosine 3',5'-cyclic monophosphorothioate, 4-cyano-3-methylisoquinoline,
15 1-(5-isoquinolinesulfonyl)-2-methylpiperazine, N-[2-(methylamino)ethyl]-5-isoquinoline sulfonamide, isoquinolinesulfonamide, N-(2-aminoethyl)-5-isoquinolinesulfonamide, N-[2-((p-bromocinnamy) amino)ethyl]-5-isoquinolinesulfonamide and (5-isoquino linesulfonyl)piperazine.

20 19. The composition according to claim 16, wherein the inhibitor of protein kinase C is selected from the group consisting of 2-[1-(3-dimethylaminopropyl)-1H-indol-3-yl]-3-(1H-indol-3-yl)-maleimide, 2-[1-[2-(1-methylpyrrolidino) ethyl]-1H-indol-3-yl]-
25 3-(1H-indol-3-yl)maleimide, 2-[1-(3-aminopropyl)-1H-indol-3-yl]-

3-(1H-indol-3-yl)maleimide, 2,3-bis(1H-indol-3-yl)maleimide and 2,3-bis(1H-indol-3-yl)-N-methylmaleimide.

20. The composition according to claim 16, wherein the activator
5 of Gi protein is selected from the group consisting of N₆-cyclopentyladenosine, 5-chloro-N₆-adenosine, 2-[p-(2-carboxyethyl) phenethylamino]-5'-N-ethylcarboxamidoadenosine, oxymetazoline, prazosin, 2-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-4,4-dimethyl-(2H,4H)-isoquinoline-1,3-dione,
10 cannibinol, MGSA, 3-aminopropylphosphinic acid, galanin, quisqualate, sumatriptan, melatonin, (5,7,8)-(-)-N-methyl-[7-(1-pyrrolidinyl)-1-oxaspiro(4,5)dec-8-yl]benzeneacetamide and pertussis toxin.

15 21. The composition according to claim 16, wherein the senescent cell is derived from human cell.

22. The composition according to claim 21, wherein the human cell is fibroblast.

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23. A method for modulating cellular senescence in a patient in need thereof, comprising administering to the patient the effective amount of an inhibitor of adenylyl cyclase, an inhibitor of protein kinase A, an inhibitor of protein kinase C
25 or an activator of Gi protein.

24. The method according to claim 23, wherein the inhibitor of adenylyl cyclase is selected from the group consisting of 2',5'-dideoxyadenosine, cis-N-(2-phenylcyclopentyl)azacyclotridec-1-en-2-amine and 9-(tetrahydro-2'-furyl)adenine.

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25. The method according to claim 23, wherein the inhibitor of protein kinase A is selected from the group consisting of adenosine 3',5'-cyclic phosphorothiolate, 8-bromo-adenosine 3',5'-cyclic monophosphorothioate, 4-cyano-3-methylisoquinoline, 1-(5-isoquinolinesulfonyl)-2-methylpiperazine, N-[2-(methylamino)ethyl]-5-isoquinolinesulfonamide, isoquinolinesulfonamide, N-(2-aminoethyl)-5-isoquinolinesulfonamide, N-[2-((p-bromocinnamy)amino)ethyl]-5-isoquinolinesulfonamide and (5-isoquinolinesulfonyl)piperazine.

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26. The method according to claim 23, wherein the inhibitor of protein kinase C is selected from the group consisting of 2-[1-(3-dimethylaminopropyl)-1H-indol-3-yl]-3-(1H-indol-3-yl)-maleimide, 2-[1-[2-(1-methylpyrrolidino)ethyl]-1H-indol-3-yl]-3-(1H-indol-3-yl)maleimide, 2-[1-(3-aminopropyl)-1H-indol-3-yl]-3-(1H-indol-3-yl)maleimide, 2,3-bis(1H-indol-3-yl)maleimide and 2,3-bis(1H-indol-3-yl)-N-methylmaleimide.

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27. The method according to claim 23, wherein the activator of Gi protein is selected from the group consisting of N₆-

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cyclopentyladenosine, 5-chloro-N₆-adenosine, 2-[p-(2-carboxyethyl) phenethylamino]-5'-N-ethylcarboxamido adenosine, oxymetazoline, prazosin, 2-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-4,4-dimethyl-(2H,4H)-isoquinoline-1,3-dione, 5 cannibinol, MGSA, 3-aminopropylphosphinic acid, galanin, quisqualate, sumatriptan, melatonin, (5,7,8)-(-)-N-methyl-[7-(1-pyrrolidinyl)-1-oxaspiro(4,5)dec-8-yl]benzeneacetamide and pertussis toxin.